



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

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Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

INTERVIEW SUMMARY

All participants (applicant, applicant's representative, PTO personnel):

(1) ERMA CAMERON (3) DARRELL W. KESLER
(2) Eric S. Wright (4) HAROLD R. Potts
Date of Interview 1/23/2003 (5) Gregory M. Friedlander

Type: ☐ Telephonic ☒ Personal (copy is given to ☒ applicant ☐ applicant's representative)

Exhibit shown or demonstration conducted: ☒ Yes ☐ No If yes, brief description: wood treated with the
claimed process

Agreement ☐ was reached. ☒ was not reached.

Claim(s) discussed: all

Identification of prior art discussed: JP 08-318509

Description of the general nature of what was agreed to if an agreement was reached, or any other comments:

The differences between the conventional prior art wood
treatments, many of which are sol-gel processes, and the claimed
invention were discussed. JP 08-318509 was also compared
to the claimed invention.

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

1. ☒ It is not necessary for applicant to provide a separate record of the substance of the interview.

Unless the paragraph above has been checked to indicate to the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a response to the last Office action has been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW.

2. ☐ Since the Examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, objections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the interview unless box 1 above is also checked.

Examiner's Note: You must sign this form unless it is an attachment to another form.

FORM PTOL-413 (REV.1-96)

Manual of Patent Examining Procedure, Section 713.04 Substance of Interview must Be Made of Record

A complete written statement as to the substance of any face-to-face or telephone interview with regard to an application must be made of record in the application, whether or not an agreement with the examiner was reached at the interview.

§1.133 Interviews

(b) In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for response to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

§ 1.2. Business to be transacted in writing. All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete a two-sheet carbon interleaf Interview Summary Form for each interview held after January 1, 1978 where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks in neat handwritten form using a ball point pen. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below.

The Interview Summary Form shall be given an appropriate paper number, placed in the right hand portion of the file, and listed on the "Contents" list on the file wrapper. The docket and serial register cards need not be updated to reflect interviews. In a personal interview, the duplicate copy of the Form is removed and given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephonic interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the telephonic interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Serial Number of the application
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (personal or telephonic)
- Name of participant(s) (applicant, attorney or agent, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the claims discussed
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). (Agreements as to allowability are tentative and do not restrict further action by the examiner to the contrary.)
- The signature of the examiner who conducted the interview
- Names of other Patent and Trademark Office personnel present.

The Form also contains a statement reminding the applicant of his responsibility to record the substance of the interview.

It is desirable that the examiner orally remind the applicant of his obligation to record the substance of the interview in each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check a box at the bottom of the Form informing the applicant that he need not supplement the Form by submitting a separate record of the substance of the interview.

It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview:

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner. The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he feels were or might be persuasive to the examiner,
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete or accurate, the examiner will give the applicant one month from the date of the notifying letter or the remainder of any period for response, whichever is longer, to complete the response and thereby avoid abandonment of the application (37 CFR 1.135(c)).

Examiner to Check for Accuracy

Applicant's summary of what took place at the interview should be carefully checked to determine the accuracy of any argument or statement attributed to the examiner during the interview. If there is an inaccuracy and it bears directly on the question of patentability, it should be pointed out in the next Office letter. If the claims are allowable for other reasons of record, the examiner should send a letter setting forth his or her version of the statement attributed to him. If the record is complete and accurate, the examiner should place the indication "Interview record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

I, M. Gopal Nair, hereby declare that:

I currently serve as Professor of Biochemistry and Molecular Biology at the University of South Alabama College of Medicine. I am a Senior Scientist and I am also the Director of the Drug Development Laboratory at the University of South Alabama Cancer Center and a Scientist at the Comprehensive Cancer Center at the University of Alabama in Birmingham.

I have served as Chairman of the Department of Biochemistry and Molecular Biology of the college of Medicine for two years beginning 1990, and then served as Vice-Chairman through September 2001. I have received numerous Awards from National Cancer Institute, American Cancer Society and American Heart Association for the past two decades to pursue my drug development efforts. I have advised Private corporations, including BioNumerik Pharmaceuticals, Inc. on the procedures of writing Investigational New Drug (IND) applications, FDA regulations, conflict of Interest, compound manufacture and formulations and served as a consultant to a number of private industries. My professional peers are at the highest levels of outstanding and dedicated scientists who are leaders in their respective fields and are work at various prestigious Universities in the United States and throughout the world.

I have also served as Major Professor, Mentor, Director and Guide to the Ph.D. students throughout their career and tenure in my laboratory. Further, I have taught, directed and guided the research of a number of post-doctoral research associates who were hired by me to carry out chemical research in the areas of compound synthesis

and formulation. I have more than 160 publications. My contributions in compound synthesis and formulations are widely recognized nationally and internationally.

I am Inventor or co-Inventor of several Patents. All of my patents are new inventions developed in my laboratory as potential treatments for human diseases. I have been invited several times by Federal Government Agencies to serve as a member on committees on drug development for cancer, AIDS and other diseases.

I have had extensive practical and theoretical experience with protection and deprotection of amino, hydroxyl and carboxyl groups of complex organic molecules by silylation, phosphorous chemistry and hydroboration.

This experience is relevant in the analysis of the patentability of the application 09/885,642 because this application deals with silicon and boron chemistry with emphasis placed on the reaction of hydroxyl groups of various wood molecules. Further it deals with the novelty, chemical differences and advantages of the present invention as opposed to the cited, but not relied up on up on prior art._

I have experience in Patent filing and prosecution in the United States and world-wide. I have personally drafted applications (including claims) for a number of United States and international Patent applications. The prosecution of each of my Patent applications resulted in allowable claims and issued Patents.

For further details regarding my experience, please see my curriculum vitae, which is attached for the Examiner's convenience.

Collectively the above knowledge and experience have provided me with the required expertise to comment on the Patentability of the claims of the '642 application.cited documents I have personal knowledge of wood treatment invention

of the '642 application and have personally evaluated the theoretical mechanism by which the reactions take place

The invention does provide simultaneous hydrophobicity, fire retardancy and microbial protection to wood treated by Applicant's invention.

DISTINGUISHING THE CLAIMS OF THE '642 APPLICATION

Distinguishing Over JP 8-318509 To Kokai

Applicant's Claimed Element	Disclosure Of Kokai	Claimed Elements Not Disclosed	Why Applicant's Invention Is Distinguished Over Kokai
Pro-catalyst: Halogenated alkylsilanes	No disclosure of the use of halogenated alkylsilanes		No halogenated alkylsilanes in formula
HCl produced on contact with wood	No HCl		Lack of mineral acid formation
Dialkyl dihalogenated silanes as pro-catalysts	No halogenated silanes of any kind		
Tri-alkyl monohalogenated silanes as pro-catalyst	No halogenated silanes whatsoever		Applicant's wood treatment formula is distinctly different and unexpected in composition and procedures

Distinguishing Over JP 8-318509 To Kokai In View Of US 3,682,675 To

Meyers

Applicant's Claimed Element	Disclosure Of Kokai	Disclosure Of Meyers	Claimed Elements not disclosed	Why Applicant's Invention Is Distinguished Over Kokai In View of Meyers
Pro-catalyst in the formula	No pro-catalyst in the treatment formula	No pro-catalyst in the treatment formula		No similarity in the treatment formula that comes in contact with wood.

**Distinguishing Over JP 8-318509 To Kokai In View Of The Disclosure Of
Ogiso**

Applicant's Claimed Element	Disclosure Of Kokai	Disclosure Of Ogiso	Claimed Elements not disclosed	Why Applicant's Invention Is Distinguished Over Kokai In View of Ogiso
The formula consists of the crucial halogenated mono, di or trialkylsilane.	No halogenated alkylsilane in the formula	Uses SOL-GEL method with ultrasound Sol-Gel is an oligomer of ill-defined composition. Does not have any halogenated pro-catalyst in the treatment formula		The applicant's formula is designed on the inclusion of a halogenated mono, di or trialkylsilane in an otherwise well defined stable chemical formula. For this single reason alone the applicant's formula is novel and unexpected.

Distinguishing Over JP 8-318509 To Kokai In View Of US 5,652,026 To Saka

Applicant's Claimed Element	Disclosure Of Kokai	Disclosure Of Saka	Claimed Elements Not Disclosed	Why Applicant's Invention Is Distinguished Over Kokai
Halogenated mono, di and trialkylsilanes as pro-catalysts	None	Mixtures of oligomers of boron, silicon and phosphorous of ill-defined composition		There are no similarities of the instant formula with the oligomer gels of Saka

SAKA(U.S. 5,652,026)	KELSOE APPLICATION
Saka Formula is entirely different. It has no relation to the kelsoe formula. The formulae are mixtures of p lyomers made outside the wood in a separate chemical process. This formula has no resemblance or similarity with the Kelsoe composition at all.	Hydrophilic solvent (ethanol) is used Completely homogenous and stable composition that is crystal clear and extremely compatible with all kind of wood and wood products.
	Mixes completely with water
Wood needs to be CONDITIONED prior to treatment with unrelated composition. Acetone extraction with a soxhlet for several hours should precede water conditioning of wood to desired moisture level. This is a time consuming and expensive procedure.	Will penetrate both wet and dry wood No conditioning of wood is required.
	No evolution of any gases. Environmentally safe.
	Does not contribute to anti-microbe protection by boron
	Forms non-leachable boron/silicon matrix on all parts of treated wood.
	Simultaneous microbial, water and fire resistance are obtained by the Kelsoe composition.
	Formula contains a mixture of three components: An activatable silicon additive, an activatable boron reagent and a pro-catalyst that on contact with wood molecules activates the silicon additive and boron reagent simultaneously and exothermically to form stable covalent bonds of boron and silicon atoms with wood molecules containing hydroxyl groups.
SAKA et al. JP2962191(1999); 08318509 (1996)	

<p>Needs hydrolysis, thermal decomposition and poly-condensation of the formula to be partially effective. Even after these three discreet steps applied to wood after treatment 6% of metal oxide is leached out indicating that the metal is NOT covalently attached to wood molecules.</p> <ol style="list-style-type: none"> 1. The wood piece needs to be in contact with formula under vacuum (15 mmHg) for three days. 2. Needs heating at 65 degree centigrade for 24 hours (endothermic process; heat must be provided) to decompose. 3. Then heating required for 24 hours at 105 degrees. A highly endothermic reaction for poly-condensation. 	<ol style="list-style-type: none"> 1. No vacuum required 2. No heating of any amount required 3. The reaction is spontaneous and exothermic 4. The pro-catalyst in the formula facilitates covalent bond formation between hydroxy groups of wood molecules and the metal atoms (boron and silicon) to form permanent bonds. 5. No leaching of metal takes place 6. The presence of the pro-catalyst in the instant patent formula aids spontaneous reaction of wood hydroxyl groups with metal atoms without the need of: Hydrolysis, pyrolysis and poly-condensation all highly endothermic processes required by the teachings of Saka Patent 08318509.
<p>SCHULDT et al. 1995:14754</p> <p>A laboratory process to protect hydroxyl groups of cellulose with trimethylsilyl group is described. The technology does not teach the use of a mixture of boron and silicon compounds to impart hydrophobicity, microbial resistance and fire retardancy to wood or wood products. The technology is not relevant to the teachings of the instant patent.</p>	<p>This well-known laboratory procedure is not relevant to the instant patent application.</p>

In U.S. Patent 5,652,026 to Saka *et al.*, the disclosure technology treats wood with a methylsiloxane oligomer which contains phosphorous and/or boron. These are high molecular weight co-polymers that need to be prepared separately from trialkoxysilanes and other reagents by heating and diluting. The material to be applied on to wood is not an alkyltrialkoxysilane but a pre-prepared copolymer. Saka does not disclose Applicant's claimed composition.

The wood to be treated by the Saka treatment is moisture conditioned first by soxhlet extraction with acetone, a very expensive procedure followed by exposure to

moisture to the desired water content. This conditioned wood is then dipped for three days in the oligomer formula in methanol under vacuum. Essentially the oligomer is forced to be drawn in to the pores of wood by mechanically applied vacuum and the methanol is simultaneously removed. The wood then undergoes heat treatment at 65 degrees for one day and then at 105 degrees for another day. This wood had a weight gain of 11.3%; however on exposure to water for four hours more than one half of the silicon (7.5%) was leached out indicating that the silicon is not bonded to the wood in spite of prolonged and expensive curing of the wood at high temperatures after treatment.

Saka's technology of using the silicon oligomers followed by curing the wood at high temperatures to obtain fire retardancy is not related to the Fossil Rock technology as described above.

MECHANISM OF REACTION OF KELSOE FORMULATION WITH WOOD vs.

SOL-GEL PROCEDURE OF SAKA:

Applicant's the '642 application is unexpected, new and novel. For example if one evaluate the make-up of the reacting formula of the sol-gel technology with wood vs. the reacting formula of the '642 application there are no similarities at all.

Saka's disclosure is a mixture of un-reactive gel comprising of oligomers made soluble in an aqueous medium (SOL-GEL formula).

Saka's treatment is un-reactive on contact with wood.

Saka's disclosed technology is based upon **SOL-GEL** technology. The term SOL-GEL refers to ____1. Making a gel like substance of undefined chemical composition by hydrolyzing a mixture of boron, silicon and phosphorous reagents with

water which is a mixed oligomer, in a reaction vessel outside the vicinity of any material to be treated.

2. The above gel is then made soluble in an aqueous organic solvent . This solution no longer contains or have any similarities with the reagents used as wood treatments in the instant patent. This is the wood treatment formula of the Gel-Sol technology of Saka.

4. The wood to be treated is separately extracted with acetone in a special complex apparatus known as the soxhlet to remove water. The wood is then dried and exposed to moisture to get the desired moisture content for the wood to be treated.
5. The wood is then placed in a chamber and vacuum is applied for approximately three days to "evacuate" the wood
6. The evacuated wood while in vacuum is then exposed to the solubilized oligomer gel formula to have the formula enter the wood. The wood is then removed after forced impregnation under vacuum and then dried at 60 degrees.
7. No reaction has yet taken place among wood molecules and the oligomer formula.
8. The wood is then heated at 105 degrees for another 24 hours to make the reaction work at least partially. Both silicon and boron leaches out of the wood in significant amounts after pyrolysis.
9. SOL-GEL stands for Soluble Gel.

The composition of the formula consists of oligomers of polysiloxanes prepared from hydrolysable silicon, boron and phosphorous compounds that are treated with water and hydrolysed to oligomers of unknown composition. This mixtures of oligomers are then

dissolved in methanol/water to make the formula to treat wood. Saka utilizes a mixture of oligomers in aqueous methanol prepared outside wood prior to treatment. This formula is not related to Applicant's invention.

It does not matter where the hydrolysis take place. Saka's oligomers whether outside or inside the wood are unable to react with wood molecules. The Saka gel oligomerizes under the required condition of heating for prolonged periods (24 hours at 60 degrees and another 24 hors at 105 degrees). In order for the formula to penetrate wood of 1.0 mm thickness a vacuum must be applied for three days. In addition the wood piece must be preconditioned with soxhlet extraction and then moisture conditioned. The entire procedure is so cumbersome and expensive that in all probability will not result in profitable industrial application.

The '642 application on the other hand has a well-defined chemical formula that is completely homogeneous and stable. No expensive and time consuming (soxhlet extraction with acetone and then moisture conditioning) preconditioning of wood is needed for the reactions to occur. The formula is absorbed to ALL parts of wood by simple contact (dipping, brushing or spraying). No application of vacuum is necessary. Once absorbed and in contact with wood molecules having hydroxy groups (cellulose, lignins etc.) the pro-catalyst present in Kelsoe patent formula releases hydrogen chloride in catalytic amount that in turn activates the silicon and boron additives for reaction with hydroxyl groups of wood molecule resulting in covalent bond formation. These reactions are spontaneous and exothermic as opposed to the highly endothermic conditions required for the SAKA technology. Once the catalyst is released on contact with hydroxyl groups of wood molecules, the Kelsoe formula is self activated to initiate a chain reaction

that eventually results in the covalent bonding of both boron and silicon to wood molecules. Therefore the boron and silicon are not leached out as experimentally verified in the specification section of the Kelsoe application.

The Saka method that relies on the Sol-Gel procedure is of theoretical interest but it is useless as a profitable and viable method for wood treatment in the lumber industry. Saka method teaches impregnation of a gel prepared separately outside the wood, by hydrolyzing a hydrolysable silicon compound with or without addition of hydrolysable phosphorous or boron compound to form un-reactive mixed gels of undefined composition. This gel is then dissolved again outside the wood to be treated in a mixture of methanol water. Therefore the Saka formula is a solution of an un-reactive mixed gel of unknown composition. The Kelsoe formula is a crystal clear solution the composition of which is well defined and which on contact with wet or dry wood results in spontaneous and instant mild exothermic reaction to render wood simultaneous hydrophobicity, fire retardancy and microbial resistance.

Applicant's claimed invention is a stable crystal clear solution consisting of a pro-catalyst and a catalytically activatable silicon reagent with or without an appropriate boron additive. A pro-catalyst is ___ a compound that on demand is converted to a catalyst. The demand in the present invention is exposure to hydroxyl groups of various wood molecules on contact. A catalytically activatable reagent is a reagent that is unreactive unless activated by the catalyst. In the present invention a mineral acid is produced in situ on instant contact with wood molecule that in turn activates the boron and silicon additives for instant reaction with wood molecules to form covalent bonds.

The pro-catalyst used in the instant formula is methyltrichlorosilane that on contact with hydroxyl groups will generate a strong mineral acid that in turn will activate the silicon and boron additives for instant covalent bond formation with wood molecules via the hydroxyl oxygen. No where in the cited up on prior art there is a technology with the instant formation of a catalyst from a pro-catalyst that in turn will activate unreactive silicon and boron additives for instant reaction with wood molecule on contact to provide hydrophobicity, fire retardancy and microbial resistance. This expert respectfully submit that the Kelsoe technology is new, novel and unexpected and is patentable over the prior art teachings

Different from the Saka procedure which requires evacuation of conditioned wood for three days at 15mm/Hg, Applicant's invention penetrates both wet and dry wood on contact (dipping, spraying or brushing) and instantly reacts with wood to impart the desired properties. For these reason alone this expert respectfully submit that the Kelsoe composition to treat wood is patentable over the sol-gel procedures of Saka.

Applicant's invention imparts hydrophobicity, fire-retardancy and microbial resistance to both wet and dry wood just by contact. This unprecedented property is built in to the formula by careful theoretical design. Once the formula comes in contact with wood molecules having hydroxyl groups the pro-catalyst instantly reacts with hydroxy groups generating a mineral acid exothermically that protonates the alkoxyl groups of the silicon additive and boron additive. The mineral acid does not escape the wood as gas because of its relative small amounts and the large amount of additives to be protonated. Protonation of the alkoxyl groups of the additives activate them for instant reaction with

wood hydroxy molecules that results on covalent bond formation of silicon and boron atoms with the oxygen atoms of the wood permanently.

The entire wood is thus treated permanently in ONE STEP; JUST CONTACT!

Therefore from a mechanistic point alone the technology is novel, new and unprecedented. The composition claims recited in the Kelsoe application are patentable over the cited documents taught in SAKA patents.

Fossil Rock Company has responded to various draw-backs of previous silicon and boron based technologies for potential wood treatment. The technologies cited by the U.S.P.T.O. do not anticipate and do not make obvious Applicant's claims. None of the cited technologies disclose all of the elements claimed by the Applicant's, and they do not teach or suggest Applicant's claimed invention (discussed in detail below). Further, the cited technologies have not achieved commercial success. The cited documents The cited methods disclosed are different from the technology claimed by Applicant's, and are clumsy, difficult to carry out and extremely expensive. On the other hand the '642 application is simple, convenient, cheap, **new, novel and unexpected**.

'642 application differs entirely from the above cited documents technology with respect to the composition in the following ways:

- Kelsoe composition is chemically well **defined** and identified.
- Kelsoe composition does not make use of aqueous solutions, **anhydrous organic solvent** is required for the composition.
- Kelsoe composition , in one embodiment, utilizes a **halogenated** silane component as a pro-catalyst. [The concept of pro-catalyst is **novel and unexpected** in wood industry.

- Kelsoe composition enters wood without prior conditioning or application of vacuum for several days
- Kelsoe composition **instantly reacts with wood hydroxyl groups on contact** and activates the accompanying reagents to form silicon-oxygen **covalent bonds** not only on the surface but also within the wood.
- Kelsoe composition requires no prior drying of wood or no drying of wood after treatment to be effective.

Various Kelsoe formulations described herein are unique with respect to defined and pure ingredients and the formula must have a **halogenated silane** and a **non-aqueous** organic solvent to be effective. None of the cited documents describes the use of a halogenated silane as a pro-catalyst to activate additives for instant reaction within the wood with wood molecules to form stable covalent bonds.

For these reasons and others the technology described in the instant application is novel, unprecedented and unexpected from SAKA teachings. There fore I respectfully submit that the technology described in the Kelsoe application is patentable over the cited up on cited documents of SAKA and others.

Respectfully submitted.

M. G. Nair, Ph.D.

Professor

CURRICULUM VITAE
Madhavan G. Nair

PERSONAL INFORMATION:

BORN: Kerala, INDIA.

Marital Status: Married, Two Children (06/10/76 & 04/24/78)

CURRENT POSITION TITLES:

Professor of Biochemistry & Molecular biology

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Senior Scientist

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CITIZENSHIP:

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EDUCATION:

B. Sc. University College, Trivandrum, India (1959)

M. Sc. University College, Trivandrum, India (1962)

Ph. D. Florida State University, Tallahassee, Florida (1969)
Professor Werner Herz

Post-Doctoral Training:

University of Tennessee, Med. Units (Post-Doctoral) 1969-1970.
Cancer Chemotherapy Program. Professor F.C. Chang.

HONORARY:

NSF Pre-doctoral Fellow

Cover Legend, Cancer Research, April 15, 1992

Who is Who in Science and Technology

PROFESSIONAL SOCIETY MEMBERSHIPS:

American Society for Biochemistry and Molecular Biology

American Society for Pharmacology and Experimental Therapeutics

American Chemical Society

American Association for Cancer Research

CONSULTANTSHIPS:

(1) Shell Development Company, Modesto, California (1979-1983)

(2) New England Nuclear, Boston, Mass. (1976-1980)

(3) Scientific Consultant, National Cancer Institute (1983-1996)

(4) American Radiolabeled Chemicals, Inc., St. Louis, MO (1984-1999)

(5) Burroughs Wellcome Co., Research Triangle Park, NC (1987-1990)

(6) FMC- Corporation, Princeton, New Jersey (1992)

(7) BioNumerik Pharmaceuticals, Inc. San Antonio, Texas (1993-1997 & 1998-1999)

(8) Fossil Rock, Inc. (2000- present)

ACADEMIC QUALIFICATIONS:

PROFESSIONAL APPOINTMENTS:

(June 1990-Jan 1992)	Interim Chairman Department of Biochemistry, University of South Alabama, College of Medicine
(Feb, 1992-2001)	Vice Chairman , Department of Biochemistry, University of South Alabama College of Medicine.
(1980-present)	Professor, Department of Biochemistry and Molecular Biology, University of South Alabama, College of Medicine
(1984-present)	Senior Scientist, University of South Alabama Cancer Center
(1986-present)	Senior Scientist, University of Alabama Comprehensive Cancer Center, Birmingham,

PREVIOUS APPOINTMENTS:

(1962-1963) **Scientific Officer**, Bhaba Atomic Research Center, Trombay, India

(1963-1964) Research Chemist, CIBA Pharmaceuticals, Bombay, India

(1971-1973) Assistant Professor of Medicine, Pediatrics and Chemistry, University of Alabama, Birmingham

(1973-1976) Assistant Professor, Department of Biochemistry, University of South Alabama College of Medicine

(1977-1980) Associate Professor, Department of Biochemistry, University of South Alabama College of Medicine

COMMITTEE APPOINTMENTS:

(1977-1978)	Biohazards Committee
(1979-1980)	Radiation Safety Committee
(1980-1983)	Admissions Committee (Medical Students)
(1980-1983)	Waterman Scholarship Committee
(1980)	Committee on Faculty Reorganization
(1982-1992)	Member, Cancer Coordinating Committee
(1983-1984) Evaluation	Faculty Committee on Appointments, Promotion and
(1983-1986)	Admission Committee (Graduate Students)
(1984)	Member, Faculty Senate
(1984-1986)	Member, Committee on Committees
(1986-1991)	Member, Cancer Coordinating Committee
(1987-1989) Committee	Member, Student Evaluation and Promotions
(1987) Committee	Member, Medical Alumni Association Scholarship
(1989-1993)	Member, Patent Committee, College of Medicine
(1989-1998) Center. College of Medicine	Member, Advisory Committee, Mass Spectrometry
(1990-1992)	Member, Biochemistry Curriculum Committee
(1990-92) Alabama, College of Medicine	Member, Executive Council , Univ. of South
(1990-92) Sciences	Member, Executive Committee , Basic Medical
(1990-1992)	Member, Executive Committee , Graduate Program

in Basic Medical Sciences

(1993-1997) Chairman, Patent Committee, College of Medicine

(1993-1995) Member, Faculty Committee on Appointments and Promotion

1999- present Member, Faculty Grievance committee

EDITORIAL REVIEW (Ad Hoc)

Journal of Medicinal Chemistry

Journal of Organic Chemistry

Cancer Research

Other Journals

TEACHING ASSIGNMENTS:

BCH 121 - Medical Biochemistry

GMS 521 - Comprehensive Biochemistry

GMS 520 - Comprehensive Biochemistry Coursemaster, GMS 510 and

GMS 521 - 1980-1985

GMS 520 - Physical Biochemistry

GMS 620 - Enzymes and Proteins

POST-DOCTORAL FELLOWS DIRECTED:

American Cancer Society

Dr. S.Y. Chen

Dr. Maryam Gazala

Dr. S.R. Adapa

Dr. V.S. Sloan

National Cancer
Institute

Dr. B.R. Murthy

Dr. T. Nieduzak

Dr. Li Ming Yang

Dr. S.B. Patil

Dr. Shu Wen Li

Dr. Ann Abraham

GRADUATE Ph.D. DISSERTATIONS DIRECTED AS MAJOR PROFESSOR:

Ann Abraham (1986-1991). Ph.D.

Anjali Desai (1987-1994). Ph.D.

Li Liu (1992-96). Ph.D.

NATIONAL& FEDERAL COMMITTEES

NIH, Medicinal Chemistry Study Section (1983)

NCI, Site Visit Team, Yale University (1983)

NCI, Site Visit Team, Princeton University (1983)

NCI, Grant Review Group, Folate Symposium (1986)

NCI, Member Review Group, Outstanding Investigator awards (1987)

NIAID, Member, Study Section (Ad Hoc). National Co-operative Drug
Discovery group for the treatment of AIDS (1987)

NCI, Member, Site Visit Team, St. Jude Children's Hospital (1987)

NCI, Member, Contract Technical Review Group (Ad Hoc) Preclinical
Pharmacology of Anti-AIDS Agents (1987)

NIAID, TRIAGE Subcommittee (Member) (1988)

NIAID, Review Group (Ad Hoc) National Co-operative Drug Discovery
Group for the Treatment of Aids (1988)

NIAID, Review Group. Synthetic vaccine adjuvants (1989)

NCI, Member, Experimental Therapeutics Study Section (Ad Hoc 1991)

Member, Organizing Committee, 10th International Symposium on the

Chemistry and Biology of Pteridines

NIH, Nominated, Physiological Sciences Study Section (Declined)**

Member, Experimental Therapeutic Study Section, (1992 - 1995)

Chair, ET-1 Study Section (AHR-S1) 1992

Member, Scientific Advisory Committee, 11th International Symposium on Pteridines, Germany (1997)

RAID Advisory Committee, National Cancer Institute [declined]**

***** Due to a significant hearing difficulty no further invitations to serve on Federal and National Committees were accepted.***

AWARDS: RESEARCH GRANTS AS PRINCIPAL INVESTIGATOR:

(1975-1976) Burroughs Wellcome Company: A search for new bacteriostatic agents. (\$6,974)

(1975-1976) Intramural Research Award: Cancer Chemotherapy: Substrates of dihydrofolate reductase. (\$4,000)

(1976-1978) American Cancer Society: Cancer chemotherapy: substrates of dihydrofolate reductase. (\$43,404)

(1978-1979) Alabama Heart Association: Search for a hypocholesteremic drug from nature. (\$8,741)

(1978-1980) American Cancer Society: Cancer chemotherapy: Substrates of dihydrofolate reductase. (\$49,212)

(1979-1981) National Cancer Institute: Cancer chemotherapy: New folate analogs. (\$38,732)

(1980-1981) American Cancer Society: Cancer Chemotherapy. (\$24,262)

(1981-1983) National Cancer Institute - Cancer Chemotherapy: New folate analogs. (\$87,689)

(1983-1986) National Cancer Institute: Poly-gamma-glutamation and antitumor activity of antifolates. (\$175,063)

(1984-1987) National Cancer Institute: Cancer Chemotherapy: New folate analogs. (\$239,529)

(1987-1990) National Cancer Institute: Poly-gamma-glutamation and antitumor activity of antifolates. (\$213,208)

(1988-1990) National Cancer Institute: Cancer Chemotherapy: New Folate Analogues. (\$218,658)

(1988-1989) Burroughs Wellcome Co. Antitumor Agents. Inhibitors of Purine and Pyrimidine Biosynthesis. (\$42,000)

(1989-1990) Burroughs Wellcome Co.: Potential Antitumor Agents. (\$43,700)

(1992-1993) NIH, 10th International Pteridine Symposium \$10,000.00.

(1990-1995) NIH, Cancer chemotherapy: New folate analogues. (CA 27101-13) Total award.(\$1,229,000)

(1990-1996) Direct Costs/year: \$154,346 \$160,520 \$166,941 \$173,619 \$180,564

(1993-1997) BioNumeric Pharmaceuticals. Pre-clinical & clinical development of MAM/MEDAM/MMTX/TAF technologies . Total Direct Cost.\$233,025 [indirect \$77,675]

(1995-1997) American Heart Assoc. (Alabama Affiliate). Effect of Resveratrol on serum lipids in the rat. \$60,000.00

(1996-1999) American Cancer Society. Metabolism blocked antifolates & Novel GARFT Inhibitors. Total Cost \$300,000

(1997-2000) NIH, Cancer Chemotherapy: New Folate Analogs. Total cost. \$585,129.00

(2001-2002) Fossil Rock, Inc.

OTHER HONORS:

- Listed in
- a) American Men and Women of Science.
 - b) Innovators of American Technology.

c) **Cancer Research, Cover Legend April 15,1992.**[For the discovery of Antifolate polyglutamates and its implication in Metabolism-based antifolate drug design]

RESEARCH INTERESTS:

The Chemistry and Biology of Antifolates.

Mechanism and Metabolism-based antifolate drug Design and Development.

Cancer chemotherapy: Design, Synthesis and Evaluation of Potential Anti-cancer Agents. **Drug development.**

Metabolically Stable (inert) DHFR Inhibitors as Antimicrobials [opportunistic infections in AIDS]

Metabolism of Antifolate Antimetabolites

Synthetic Organic Chemistry, Molecular rearrangements, drug delivery, drug targeting and mass spectrometry of folates and antifolates.

Anti-inflammatory antifolates and their mechanism of action.

Wood Preservation technology

Food & Drug Administration [Regulatory]

1). IND 36634 (10-DAM)

- a) Wrote the IND application *except* the clinical protocol
- b) Negotiated with Dottie peace and Pilot Drug Evaluation Staff at FDA for the approval of the above IND.
- c) Received FDA approval to Qualify Nair laboratory for the preparation of the antifolate drug 10-DAM for oral administration to humans.
- d) Member of the Phase-II Clinical Trial team for evaluation of 10-DAM as an Arthritis Remettive Drug [DMARD] in arthritic patients.

MDAM-IND:

- a) Drafted the IND application of MDAM *except* the commercially available Standard Clinical Protocol for anti-cancer drugs.

- b) Advised Dr. Frederick H. Hausheer, Chairman & CEO of BioNumerik Pharmaceuticals, Inc. in drafting and filing formal IND applications and on contacts at FDA
- c) Negotiated with FDA officials Chemistry, manufacturing controls and formulation procedures for MDAM that were crucial to obtain IND status for MDAM
- d) Manufactured MDAM for intravenous administration in cancer patients for Phase-I clinical trial of MDAM.
- e) Performed bulk drug synthesis of MDAM, formulated MDAM for administration to cancer patients.
- f) Quality control of MDAM (endotoxin and sterility) for intravenous administration to cancer patients.
- g) Developed a Master File for MDAM for IND application.
- h) Developed Phase-II clinical protocol for 5,8,10-trideaza-4'-methylene- aminopterin as an Arthritis Remettive Drug.

PUBLICATIONS

SCIENTIFIC PAPERS {Original Contributions}:

M.G. Nair and N.S. Wariyar. Photolysis of aromatic amines in carbon tetrachloride. J. Proc. Int. Chem. (India) 33:61 (1963).

Werner Herz, R.C. Blackstone and M.G. Nair. Reaction of levopimaric acid with acetylenic dienophiles. J. Org. Chem. 30:4238 (1965).

Werner Herz, R.C. Blackstone and M.G. Nair. Configuration and transformations of the lovopimaric acid-p-benzo-quinone adduct. J. Org. Chem. 32:2992 (1967).

Werner Herz and M.G. Nair. A remarkable case of intramolecular energy transfer. J. Am. Chem. Soc. 89:5474 (1967).

Werner Herz and M.G. Nair. Structure and stereochemistry of adducts of levopimaric acid with cyclopentenone and 1-cyclopentene-3,5-dione: Favorskii reaction of an enedione epoxide. J. Org. Chem. 34:4016 (1969).

M.G. Nair and F.C. Chang. Conversion of 24-methylene sterols to their Delta 24,25 isomers. Tetrahedron Letters 27:2513 (1971).

M.G. Nair and C.M. Baugh. The synthesis of pteridine-6-carboxamides, 9-oxofolic acid

and 9-oxoaminopterin. J. Org. Chem. 38:2185 (1973).

M.G. Nair and F.C. Chang. 6-hydroxy-4-stigmasten-3-one and 6-hydroxy-4-campesten-3-one. Phytochemistry 12:903 (1973).

C.M. Baugh, C.L. Krumdieck and M.G. Nair. Polygamma-glutamyl metabolites of methotrexate. Biochem. Biophys. Res. Comm. 52:27 (1973).

M.G. Nair and C.M. Baugh. The synthesis and biological evaluation of polygamma-glutamyl derivatives of methotrexate. Biochem. 12:3923 (1973).

M.G. Nair and C.M. Baugh. The synthesis and biological evaluation of isofolic acid. J. Med. Chem. 17:223 (1974).

J.I. DeGraw, R.L. Kisliuk, Y. Gaumont, C.M. Baugh and M.G. Nair, Synthesis and antifolate activity of 10-deaza-aminopterin, J. Med. Chem. 17:552 (1974).

M.G. Nair, L.P. Mercer and C.M. Baugh. The synthesis and antifolate activity of isoaminopterin. J. Med. Chem. 18:1268 (1974).

C.M. Baugh, E. Braverman and M.G. Nair. The identification of polygamma-glutamyl chain lengths in bacterial folates. Biochem. 13:4952 (1974).

M.G. Nair, P.T. Campbell and C.M. Baugh. The synthesis of 10-thiofolic acid: a potential antitumor agent. J. Org. Chem. 40:1745 (1975).

Werner Herz, M.G. Nair and D. Prakash. Rearrangements in the photolevopimaric acid series -A. Paradigm of bicyclo (2.2.0)-and bicyclo (2.2.1)-hexane chemistry. J. Org. Chem. 40:1017 (1975).

M.G. Nair, Patricia Campbell, Eleanor Braverman and Charles M. Baugh. 10-thioaminopterin: a potent anti-bacterial agent. Tetrahedron Letters 31:2745 (1975).

Werner Herz, V.S. Iyer and M.G. Nair. The reaction of enedione epoxide with base. J. Org. Chem. 40:3519 (1975).

M.G. Nair and C.M. Baugh. New folate analogs: alterations in the C9-N10 bridge region. In W. Pfeiderer, Ed.: Chemistry and Biology of Pteridines, Walter de Gruyter (Berlin, NY) pp. 505-513 (1975).

C.M. Baugh, E. Braverman and M.G. Nair. Poly-gamma-glutamyl chain lengths in some natural folates and contributions of folic acid synthesized by intestinal microflora to rat nutrition. In W. Pfeiderer, Ed.: Chemistry and Biology of Pteridines, Walter de Gruyter (Berlin, NY) pp. 465-474 (1975).

R.I. Ho, L. Corman, Johanna Ho and M.G. Nair. A simple radioassay for dihydrofolate

synthetase activity in Escherichia coli and its application to an inhibition study of new pterate analogs. Anal. Biochem. 73:493-500 (1976).

J.R. Sowers, J.M. Hershman, A.E. Pekary, M.G. Nair and C.M. Baugh. Effect of N_3 -methylthyrotropin releasing hormone on the human pituitary-thyroid axis. J. Clin. Endocrinol. Metab. 43:741-748 (1976).

J.R. Sowers, J.M. Hershman, H.E. Carlson, A.E. Pekary, M.G. Nair and C.M. Baugh. Prolactin response to N_3 -methylthyrotropin releasing hormone in euthyroid subjects. J. Clin. Endocrinol. Metab. 43:749-755 (1976).

J.R. Sowers, J.M. Hershman, H.E. Carlson, A.E. Pekary, A.W. Reed, M.G. Nair and C.M. Baugh. Dose response of prolactin and thyrotropin to N_3 -methylthyrotropin releasing hormone in euthyroid subjects. J. Clin. Endocrinol. Metab. 43:856-860 (1976).

M.G. Nair and P.T. Campbell. Folate analogs altered in the C9-N10 bridge region: 10-oxafolic acid and 10-oxa-aminopterin. J. Med. Chem. 19:825-829 (1976).

M.G. Nair and C.M. Baugh. Synthesis of 14 C-Methotrexate: [N-[p-[[2,4-Diamino-4-Deoxy-6-Pteridiny] methyl] methylamino]-Benzoyl-L- 14 C-Glutamic acid. J. of Labelled Comp. and Radio Pharm. 13:147-153 (1977).

W. Herz, V.S. Iyer, M.G. Nair and J. Saltiel. Mechanism of Intramolecular Photoreactions of Two Rigid Cyclopentenones. J. Amer. Chem. Soc. 99:2704-2713 (1977).

R.H. Hornbeak and M.G. Nair. Transport and Inhibitory Activity of New Folate Analogs in HeLa Cells. Molecular Pharmacology 14:299 (1978).

M.G. Nair, P.C. O'Neal, C.M. Baugh, R.L. Kisliuk, Y. Gaumont and M. Rodman. Folate Analogs Altered in the C9-N10 Bridge Region: Tosyl Isohomofolic Acid and N10-tosyl-isohomoaminopterin. J. Med. Chem. 21:673 (1978).

S.Y. Chen and M.G. Nair. Rearrangement Reaction of 1-Chloro-4-[p-(carbomethoxy)]-thiophenoxy-2-butanone with Potassium Phthalimide. J. Org. Chem. 43:4143-4146 (1978).

C.M. Baugh, E. Braverman, M.G. Nair, D.W. Horne, W.T. Briggs and C. Wagner. The Peracid Cleavage of 5-Methyl Tetrahydrofolic Acid at the C9-N10 Bridge. Anal. Biochem. 92:366 (1979).

J.E. Morley, T.J. Garvin, A.E. Perkary, R.D. Utiger, M.G. Nair, C.M. Baugh and J.M. Hershman. Metabolic Clearance and Plasma Half Disappearance of Time of

Exogenous TRH and Pyroglutamyl-N³-methyl-histidyl-prolineamide. J. Clin. Endocrinol. Metab. 48:377 (1979).

C.M. Baugh, L. May, E.B. Braverman and M.G. Nair. Determination of the gamma-Glutamyl Peptide Chain lengths in the Foliates by a Combined Peracid-Zinc/acid procedure. In: Chemistry and Biology of Pteridines, G.M. Brown, Ed., Elsevier, North-Holland, Inc., N.Y., pp. 219-224 (1979).

M.G. Nair, S.Y. Chen, D. Strumpf and R.L. Kisliuk. New Homofolate Analogs: Alterations in the C₉-N₁₀ Region. In: Chemistry and Biology of Pteridines, G.M. Brown, Ed., Elsevier, North-Holland, Inc., N.Y., p. 255-260 (1979).

M.G. Nair, S.Y. Chen, R.L. Kisliuk, Y. Gaumont and D. Strumpf. Folate analogs altered in the C₉-N₁₀ bridge region: 11-thiohomofolic acid. J. Med. Chem. 22:850-855 (1979).

H.R. Hornbeak and M.G. Nair. Antifolate activity of Isoaminopterin in HeLa Cells. Antimicrobial Agents and Chemotherapy 15:730-734 (1979).

M.G. Nair, C. Saunders, S.Y. Chen, R.L. Kisliuk and Y. Gaumont. Folate analogs altered in the C₉-N₁₀-bridge region 14. 11-Oxahomofolic acid, A potential antitumor agent. J. Med. Chem. 23:59-65 (1980).

M.G. Nair, S.R. Adapa and T. Bridges. Folate Analogs. 17: Synthesis of Pteric acid and 4-amino-4-deoxyptericoic acid. J. Org. Chem. 46:3152-3155 (1981).

M.G. Nair, T. Bridges, T. Henkel, R.L. Kisliuk, Y. Gaumont and F.M. Sirotnak. Folate Analogs. 18: Synthesis and antitumor evaluation of 11-oxahomoaminopterin and related compounds. J. Med. Chem. 24:1068-1073 (1981).

M.G. Nair, L.H. Boyce and M.A. Berry. Folate analogs. 19: The construction of some 6-substituted 7,8-Dihydro-8-thiopterins. J. Org. Chem. 46:3354-3357 (1981).

B.A. Domin, Y.C. Cheng and M.G. Nair. Effect of 11-Oxahomofolate and its reduced derivatives on human dihydrofolate reductase and human cells having different amounts of dihydrofolate reductase. Biochemical Pharmacology 31:255 (1982).

M.G. Nair, E. Otis, R.L. Kisliuk, and Y. Gaumont. Folate analogs. 20: Synthesis and antifolate activity of hexahydrohomofolic acid. J. Med. Chem. 26:135-140 (1983).

M.G. Nair, D.C. Salter, R.L. Kisliuk, Y. Gaumont, G. North and F.M. Sirotnak. Folate analogs. 21: Synthesis and antitumor activities of N₁₀ (Cyanomethyl)-5,8-dideazafolic acid. J. Med. Chem. 26:455-458 (1983).

M.G. Nair, O.C. Salter, R.L. Kisliuk, Y. Gaumont and G. North. Folate analogues. 22: Synthesis and biological evaluation of two analogs of dihydrofolic acid possessing a 7,8-dihydro-8-oxapterine ring system. J. Med. Chem. 26:1164 (1983).

M.G. Nair, M.K. Rozmyslovicz, R.L. Kisliuk, Y. Gaumont and F.M. Sirotnak. The nor-analogues of folic acid. In Chemistry and Biology of Pteridines. J.A. Blair, Ed. Walter de Gruyter & Co., Berlin, New York, p. 122 (1983).

R.L. Kisliuk, K.N. Rao, Y. Gaumont, R. Deschenes, K. Vestal, M. Karasik, G.F. Maley and M.G. Nair. Properties of thymidylate synthase from *Streptococcus faecium*. In Chemistry and Biology of Pteridines. J.A. Blair, Ed. Walter de Gruyter & Co., Berlin, New York, p. 375 (1983).

Y.C. Cheng, G.E. Dutschman, M.C. Starnes, M.H. Fisher, N.T. Nanavati and M.G. Nair. Activity of the new antifolate N10-propargyl-5,8-dideaza folate and its polyglutamates against dihydrofolate reductase, human thymidylate synthetase and KB cells containing different levels of dihydrofolate reductase. *Cancer Research* 45, 598 (1985).

M.G. Nair. Folate Analogues. 24: Syntheses of the antitumor agents 10-**Deazaaminopterin** and 10-Ethyl-10-**deazaaminopterin**. *J. Org. Chem.* 50, 1879 (1985).

M.G. Nair, N.T. Nanavati and B. Shane. The metabolism of 10-**Deazaaminopterin** and 10-Ethyl-10-**deazaaminopterin** in the tissues of normal mice. "Proceedings of the second workshop on folyl and antifolyl polyglutamates." I.D. Goldman, Ed. Praeger Scientific, pp. 205-213 (1985).

R.L. Kisliuk, Y. Gaumont, P. Kumar, M. Coutts, M.G. Nair, N.T. Nanavati and T.I. Kalman. The effect of polyglutamylation on the inhibitory activity of folate analogs. In "Proceedings of the second workshop on folyl and antifolylpoly glutamates." Ed. I.D. Goldman, Praeger Scientific pp. 319-328 (1985).

L.L. Samuels, L.J. Goutas, D.G. Priest, M.G. Nair, J.R. Piper and F.M. Sirotnak. Hydrolysis of 4-Aminofolyl-polyglutamates by murine host and tumor cells. In "Proceedings of the second workshop on folyl and antifolyl polyglutamates." I.D. Goldman, Eds. Praeger Scientific, N.Y., p. 233 (1985).

M. Gazala, M.G. Nair, R.L. Kisliuk, Y. Gaumont and T.I. Kalman. Folate Analogues. 25: Synthesis and biological evaluation of N10-(Propargyl) folic acid and its reduced derivatives. *J. Med. Chem.* 29, 1263 (1986).

M.G. Nair, N.T. Nanavati, I.G. Nair, M. Gazala, R.L. Kisliuk, Y. Gaumont and T.I. Kalman. Folate Analogues. 26: Syntheses and antifolate activities of analogues of 5,8-dideaza folic acid and poly-gamma-glutamyl metabolites of 10-(propargyl)-5,8-dideaza folic acid. *J. Med. Chem.* 29, 1754 (1986).

M.G. Nair and N.T. Nanavati. Folate Analogues. 27: Synthesis of 14-C labeled 10-deazaaminopterin and 10-ethyl-10-**deazaaminopterin**. *J. Labeled Comp. and Radiopharm.* 22, 24, 895 (1987).

T. Ueda, G.E. Dutschman, M.G. Nair, J.I. DeGraw, F.M. Sirotnak and Y.C. Cheng. Inhibitory action of 10-deazaaminopterin and their polyglutamates on human thymidylate synthase. *Molecular Pharmacol.* 30, 149 (1986).

P. Kumar, R.L. Kisliuk, Y. Gaumont, M.G. Nair, C.M. Baugh and B.T. Kaufman. Interaction of polyglutamyl derivatives of MTX, 10-DAAM and dihydrofolate with dihydrofolate reductase. *Cancer Res.* 46, 5020 (1986).

M.G. Nair, T.R. Toghiyani and B. Ramamurthy. A general method for the synthesis of 10-substituted-10-deazafoate analogues. Folate Analogues, part 29. "In Chemistry and Biology of Pteridines. Proceedings of the 8th International Pteridine Symposium." B.A. Cooper and M.V. Whitehead, Eds. Walter De Gruyter, Berlin, New York, pp. 45-50 (1986).

R.L. Kisliuk, Y. Gaumont, P. Kumar, M.G. Nair and B.T. Kaufman. The antifolate activity of polyglutamyl derivatives of MTX, 10-DAAM and 10-EDAAM. In "Chemistry and Biology of Pteridines." B.A. Cooper and M.V. Whitehead, Eds. Walter De Gruyter, Berlin, New York, p. 989 (1986).

M.G. Nair, N.T. Nanavati, P. Kumar, Y. Gaumont, and R.L. Kisliuk. Synthesis and biological evaluation of poly-gamma glutamyl metabolites of 10-Deazaaminopterin and 10-Ethyl-10-deazaaminopterin. *J. Med. Chem.* 31, 181 (1988).

M.G. Nair, R. Dhawan, M. Ghazala, T.I. Kalman, Y. Gaumont and R.L. Kisliuk. Folate Analogues 30: Synthesis and biological evaluation of N10-propargyl-5,8-dideaza-5,6,7,8-tetrahydrofolic acid and related compounds. *J. Med. Chem.* 30, 1256 (1987).

C. Kruger-McDermott, T.B. Johnson, R. Rej, T. Vander Hoeven, M.G. Nair and J. Galivan. The absence of gamma-glutamyltransferase activity in transport dependent MTX-resistant hepatoma cells. *Int. J. Cancer* 40, 935 (1987).

T.B. Johnson, M.G. Nair and J. Galivan. The role of folylpolyglutamate synthetase in the regulation of methotrexate polyglutamate formation. *Cancer Res.* 48, 2426 (1988).

P. Kumar, R.L. Kisliuk, Y. Gaumont, J.H. Friesheim and M.G. Nair. Human DHFR. Inhibition by polyglutamyl antifolates. *Biochem. Pharmacol.* 38, 541 (1989).

J. Thorndike, Y. Gaumont, R.L. Kisliuk, F.M. Sirotnak, B.R. Murthy, M.G. Nair and J.R. Piper. Inhibition of GAR formyl transferase and other folate enzymes by homofolate polyglutamates in human lymphoma and murine leukemia cells. *Cancer Res.* 49, 158 (1989).

J. Galivan, M.S. Rhee, T.B. Johnson, M.G. Nair, M. Bunni and D. Priest. The role of cellular folates in the enhancement of activity of the TS inhibitor, PDDF against hepatoma cells in vitro by DHFR inhibitors. *J. Biol. Chem.* 264, 10685 (1989).

J. Galivan, M.S. Rhee, T.B. Johnson, T.C. Chou, M.G. Nair and D. Priest. The enhancement of activity of PDDF and DDATHF by inhibitors of DHFR. *Adv. Enzy. Reg.* 28, 13 (1989).

M.G. Nair, B.R. Murthy, S.D. Patil, R.L. Kisliuk, J. Thorndike, Y. Gaumont, R. Ferone, D. Duch and M.P. Edelstein. Folate Analogues 31: Synthesis of the reduced derivatives of 11-~~de~~azahomofolate and their evaluation as inhibitors of GAR-formyltransferase. *J. Med. Chem.* 32, 1277 (1989).

S.D. Patil, C. Jones, M.G. Nair, J. Galivan, F. Maley, R.L. Kisliuk, Y. Gaumont, D. Duch and R. Ferone. Folate Analogues, 32: Synthesis and biological evaluation 2-desamino-2-methyl-10-propargyl-5,8-dideazafolate (DMPDDF). *J. Med. Chem.* 32, 1284 (1989).

A. Abraham, M.G. Nair, R.L. Kisliuk, Y. Gaumont and J. Galivan. Folate Analogues: 33. Synthesis of folate and antifolate poly(-glutamates by Fmoc chemistry and biological evaluation of certain methotrexate polyglutamate polylysine conjugates as inhibitors of the growth of H35 hepatoma cells. *J. Med. Chem.* 32, 711 (1990).

S.W. Li, A. Abraham, Donna Edwards and M.G. Nair. New methods for the synthesis of **quinazoline** antifolates and polyglutamyl metabolites of folate and antifolates. In "Chemistry and Biology of Pteridines" Curtius, Ghisla and Blau, Eds. Walter de Gruyter, Berlin, New York, p. 31 (1990).

M.G. Nair and I.G. Nair. Reaction of folic acid and folates analogues with acetic anhydride and pyridine. In "Chemistry and Biology of Pteridines." Curtius, Ghisla, and Blau, Eds. Walter de Gruyter, Berlin, New York, p. 81 (1990).

S.D. Patil, R.L. Kisliuk, Y. Gaumont and M.G. Nair. Synthesis and biological evaluation of 2-desamino-2-methyl-5,10-~~dide~~azatetrahydrofolate. In "Chemistry and Biology of Pteridines." Curtius, Ghisla and Blau, Eds. Walter de Gruyter, Berlin, New York, p. 1043 (1990).

M.G. Nair, A. Abraham and Susan Weintraub. Analysis of folate and antifolate metabolites by mass spectrometry. In "Chemistry and Biology of Pteridines" Curtius, Ghisla, and Blau, Eds. Walter de Gruyter, Berlin, New York, p. 181 (1989).

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Y Gaumont, R.L. Kisliuk, R. Emkey, J.R. Piper, and M.G. Nair. Folate enhancement of antifolate synergism in lymphoma cells. "In Chemistry and Biology of Pteridines". Curtius, Ghisla and Blau, Eds. Walter de Gruyter, Berlin, New York, p. 1181 (1990).

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A. Abraham, J.J. McGuire, J. Galivan, R.L. Kisliuk, Y. Gaumont and M.G. Nair. Folate analogues 34: Non-polyglutamylatable inhibitors of dihydrofolate reductase. J. Med. Chem. 34, 222 (1991).

R.L. Kisliuk, Y. Gaumont, J. Thorndike, F.A. Schmid, F.M. Sirotnak, J.R. Piper, B.R. Murthy and M.G. Nair. "Antitumor, cytotoxic and enzyme inhibitory properties of homofolates". Chapter 12. Molecular Aspects of Chemotherapy. E. Borowski and D. Shugar, Eds. Pergammon Press. (1990).

S.W. Li, M.G. Nair, D.M. Edwards, R.L. Kisliuk, Y. Gaumont, I.K. Dev, D.S. Duch, J. Humphreys, G.K. Smith, and R. Ferone. Folate Analogs, 35: Synthesis and Biological evaluation of 1-**deaza**, 3-**deaza**, and bridge elongated analogues of 10-propargyl 5,8-**dideazafolic acid** (PDDF). J. Med. Chem. 34, 2746 (1991).

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Organized the 10th International symposium on the Chemistry & Biology of folates and Pteridines.

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PRESENTATIONS:

TO PROFESSIONAL GROUPS:

(1972) 24th Southeastern Regional Meeting, American Chemical Society, Birmingham, Alabama: The synthesis of N[p[(2-amino-4-hydroxy-6-pteridiny)- amino]-methyl]benzoyl], L-glutamic acid.

(1973) 25th Southeastern Regional Meeting, American Chemical Society, Charleston, South Carolina: The synthesis and biological evaluation of poly-gamma-glutamyl derivatives of methotrexate.

(1973) Walter Reed Army Institute of Research, Antimalarial Conference, Washington, DC: Synthesis and biological evaluation of isofolic acid (Invited).

(1975) Vth International Pteridine Symposium, Konstanz, West Germany: New folate analogs alterations in the C9-N10 region (Invited).

(1975) Southeast-Southwest Regional Meeting, American Chemical Society, Memphis, Tennessee: Folate analogs altered in the C9-N10 bridge region: 10 oxafolic acid and 10-oxa aminopterin.

(1977) 173rd A.C.S. National Meeting, New Orleans, Louisiana: Isohomo Aminopterin: Synthesis and Antifolate Activity.

(1978) Alabama Academy of Science: A simple solid phase synthesis of N3-methyl thyrotropin releasing hormone.

(1978) VIth International Symposium on the Chemistry and Biology of the Pteridines, LaJolla, CA (Invited Speaker): New homofolate analogs: Alterations in the bridge region.

(1979) ACS/CSJ. Chemical Congress, Honolulu, Hawaii. Synthetic Substrates of Dihydrofolate Reductase.

(1980) 64th Annual FASEB Meeting, Anaheim, CA. Synthesis and antitumor activity of certain analogs of aminopterin.

(1980) ACS/S.W. Regional Meeting, N.O., La.: Potential Folate Antagonists.

(1981) University of Southern Mississippi (Invited). New approaches in the chemotherapy of cancer.

(1982) 66th Annual FASEB Meeting, New Orleans, LA. An alternate mechanism of dTMP biosynthesis.

(1982) VIIth International Symposium on the Chemistry and Biology of Pteridines (Invited Speaker) St. Andrews, Scotland.

(1983) Alabama Academy of Sciences. N10-Propargyl folic acid a synthetic substrate of dihydrofolate reductase.

(1984) Second Symposium on Folyl and Antifoly polyglutamates, "Metabolism of 10-**Deaza**aminopterin in mice," Airlie House, VA (invited speaker).

(1985) 189th ACS National Meeting, Miami, Florida. "A general synthesis for 10-substituted-10-**deaza** analogues of folic acid."

(1985) Univ. of South Alabama Distinguished Research Seminar. Polyglutamylation and Antitumor Activity of Antifolates."

(1986) Annual FASEB meeting. St. Louis, MO. Metabolism of 10-propargyl-5,8-**dideaza**folic acid in normal tissues of mice.

(1986) 8th International Pteridine Symposium. A general synthesis of 10-deazafolate analogues. Montreal, Canada (Invited).

(1986) ASPET-SOT meeting. "The synthesis and biological evaluation of 10-

propargyl-5,6,7,8-tetrahydro-5,8-dideazafolic acid." Baltimore, MD.

(1987) Florida A and M University, Tallahassee, Florida. Polyglutamylation and Antitumor Activity of Antifolates (Invited).

(1987) Burroughs Wellcome Company, Research Triangle Park, NC. The chemistry and metabolism of new antifolates (Invited).

(1987) University of Alabama in Birmingham, Birmingham, Alabama. The relevance of antifolate metabolism in the chemotherapy of cancer (Invited).

(1988) FASEB Meeting, Las Vegas. Methotrexate polyglutamate polylysine conjugates.

(1988) American Association of Cancer Research, New Orleans, LA. 11-**Deazatetrahydrohomofolate**: A potent inhibitor of L.casei GAR formyltransferase.

(1989) Burroughs Wellcome Company, Research Triangle Park, NC. Purine and Pyrimidine antimetabolites as potential anticancer agents. (Invited).

(1989) University of Alabama in Birmingham. Antifolates as potential antiarthritic agents (Invited).

(1989) American Association for Cancer Research, 80th Annual Meeting, San Francisco, CA. Transport and cytotoxicity of DMPDDF in H35 hepatoma cells.

(1989) American Association for Cancer Research, 80th Annual Meeting, San Francisco, CA. Synthesis of folate and antifolate polyglutamates by Fmoc chemistry.

(1989) Ninth International Symposium on the Chemistry and Biology of Pteridines, Zurich, Switzerland. New methods for the synthesis of **quinazoline** antifolates and folate and antifolate polyglutamates (Invited).

(1989) Ninth International Symposium on the Chemistry and Biology of Pteridines, Zurich, Switzerland. Reaction of acetic anhydride and pyridine with folic acid and folate analogues.

(1989) Ninth International Symposium on the Chemistry and Biology of Pteridines, Zurich, Switzerland. Synthesis and biological evaluation of 2-desamino-2-methyl-5,10-**dideazatetrahydrofolate**.

(1989) International Symposium on Biological Oxidation Systems. Bangalore, India. Evaluation of the biological oxidation of antifolates by fast atom bombardment mass spectrometry. (Invited)

(1990) Annual Meeting of the American Association for Cancer Research. Washington,

D.C. Non-polyglutamylatable antifolates.

(1991) Comprehensive Cancer Center. Ohio State University. Columbus, OH. The Clinical Relevance of the Biochemistry of Antifolates. (Invited lecture: Candidate for Associate Director. Comprehensive Cancer Center)

(1991) American Association for Cancer Research. Houston, Tx. Folate Analogs: Nonpolyglutamatable inhibitors of TS and GARFTase.

(1991) American Association for Cancer Research. Houston, TX. 10-Deazatetrahydrofolate analogues as inhibitors of GARFTase.

(1991) American Chemical Society. 4th Chemical Congress of North America. New York, NY. Receptor mediated delivery of methotrexate-insulin conjugate to H35 hepatoma and IEC-6 cells *invitro*.

(1991) New Developments in Drug Discovery and Design. Philadelphia, PA. 10-Deazaaminopterin: A new arthritis remittive drug.

(1991) New Developments in Drug Discovery and Design. Philadelphia, PA. (-Methylene-10-ethyl-10-deazaaminopterin: A very potent antitumor agent.

(1992) The Castle Group, LTD. New York, New York. Novel antifolates as therapeutic agents (Invited).

(1992) American Association for Cancer Research, San Diego, CA. 10-Formyl-**5,8,10-Trideaza** Folic Acid, FTDF: A potent inhibitor of glycinamide ribonucleotide formyl transferase.

(1992) KBL Health Care, Inc. New York, New York. Novel anticancer and anti-rheumatoid antifolates. (Invited).

(1993) Anti-neoplastic, Antimicrobial and Anti-arthritis Antifolates. Bio-numeric Pharmaceuticals, Inc., San Antonio, Texas.

(1992) Antifolates in Chemotherapy. Comprehensive Cancer Center, Medical College of Wisconsin, Milwaukee, WI. (Invited Lecture: As Candidate for Associate Director: Comprehensive Cancer Center. Job Offered; declined).

(1993) Antitumor Efficacy of Classical non-polyglutamylatable Antifolates that inhibit dihydrofolate reductase. 10th International Symposium on the Chemistry and Biology of Pteridines. Orange Beach, AL.

(1993) Evaluation of the Anti-arthritis Activity and an Alternate Synthesis of a Thiophene-substituted 10-**Deaza**aminopterin. Orange Beach, Alabama.

(1993) Antitumor Activity of Non-polyglutamylatable 10-**Deaza**aminopterins. 18th International Congress of Chemotherapy, Stockholm, Sweden.

(1994) Aldehyde oxidase mediated 7-hydroxylation of antifolates. International Symposium on biological oxidation, New Delhi, India.

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